1. A drug screening method comprising the steps of:

(a) selecting as test ligands a plurality of compounds including those not known to bind to a target protein;

(b) incubating one of said test ligands and the target protein to produce a test combination;

(c) incubating the target protein in the absence of a test ligand to produce a control combination;

(d) subjecting the test and control combinations to conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent;

(e) comparing the extent to which the target protein occurs in the folded state, the unfolded state or both in the test combination and in the control combination;

(f) repeating steps (a) through (e) with more than one thousand of said test ligands in a single day; and

(g) selecting as a ligand for said target protein any test ligand in a test combination in which the target protein is present in the folded state to a greater extent than in the control combination.

2. In the method for identifying lead compounds for possible development as pharmaceuticals by screening a plurality of test ligands for ability to bind to a target protein, the improvement which comprises:

(a) selecting as test ligands a plurality of compounds not known to bind to the target protein;

(b) admixing one of said test ligands with the target protein to produce a test combination;

(c) maintaining the target protein in the absence of a test ligand to produce a control combination;

(d) subjecting the test and control combinations to conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent;

(e) screening in excess of one thousand test ligands per day by performing steps (a) through (d) with more than one thousand ligands per day; and

(f) selecting as a lead compound any test ligand in a test combination in which the target protein is present in the folded state to a greater extent in the test combination than in the control combination.

3. A high thoughput assay for identifying lead compounds for possible development as new pharmaceuticals which comprises:

(a) selecting as test ligands a plurality of compounds including those not known to bind to the target protein;

(b) separately incubating each of said test ligands and the target protein to produce a plurality of test combinations;

(c) incubating the target protein in the absence of a test ligand to produce a control combination;

(d) subjecting each of said test combinations and the control combination to conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent;

(e) repeating steps (a) through (e) with more than 1,000 test ligands; and

(f) selecting as a lead compound each test ligand from each test combination in which the target protein is present in the folded state to a greater extent in the test combination than in the control combination.

4. The assay of claim 3 which comprises identifying at least one each of said selected ligands for possible development as a pharmaceutical.

5. The assay of claim 3 wherein said test ligands comprise small organic molecules.

6. The assay of claim 3 which comprises using steps (a) through (f) in a large-scale, systematic high throughput screening procedure.

7. The assay of claim 3 in which between 0.1% and 1% of the total test ligands are ligands of said predetermined target protein.

8. The assay of claim 3 wherein said conditions of step (d) induce the target protein to become completely denatured.

9. The assay of claim 3 wherein said conditions of step (d) are sufficient to at least partially denature the target protein.

10. The assay of claim 3 wherein the target protein comprises a polypeptide or protein implicated in the etiology of a disease.

11. An assay for use in high throughput screening a plurality of compounds against a target to identify at least one of said compounds for possible development as a pharmaceutical which comprises:

(a) selecting a plurality of test compounds not known to bind to the target protein;

(b) incubating each of said test compounds and the target protein to produce a test combination;

(c) incubating the target protein in the absence of test compounds to produce a control combination;

(d) subjecting the test and control combinations to conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent;

(e) comparing the extent of unfolding in each test combination with the extent of unfolding in the control combination;

(f) repeating steps (a) through (e) with each of said test compounds; and,

(g) selecting for possible development as a pharmaceutical any test compound in a test combination in which the target protein is unfolded to a lesser extent in the test combination than in the control combination.

12. A method for identifying at least one test ligand for possible development as a pharmaceutical agent from among a plurality of test ligands which comprises the steps of:

(a) providing as test ligands a plurality of compounds that are not known to bind to said target protein;

(b) placing at least one of said test ligands in a test well with the target protein to form a test combination;

(c) placing the target protein in a separate test well in the absence of a test ligand to from a control combination;

(d) subjecting said test combination and said control combination to conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent;

(e) determining the extent to which the target protein in the unfolded state in the test combination and in the control combination;

(f) repeating steps (a) through (e) for each of said test ligands; and,

(g) selecting as a lead compound for possible development as a pharmaceutical agent any test ligand from a test combination in which the target protein is present in the unfolded state to a greater extent in said test combination than in the control combination.

13. The assay of claim 12 which comprises using said assay to screen several thousand test ligands per day.

14. The assay of claim 12 which comprises subjecting said test combination and said control combination to conditions sufficient to cause a detectable fraction of the target protein to unfold in the absence of a test ligand.

15. The assay of claim 12 which comprises measuring the ratio of folded to unfolded target protein in the test combination and in the control combination and selecting as a lead compound any test ligand from a test combination having a higher ratio of folded to unfolded target proteins in the test combination than in said control combination.

16. In the method for selecting lead compounds for development as pharmaceuticals by identifying a ligand that binds to a predetermined target protein, the improvement which comprises:

(a) selecting as test ligands a plurality of compounds not known to bind to the target protein;

(b) incubating each of said test ligands and the target protein in a separate container to produce a plurality of test combinations;

(c) incubating the target protein in the absence of a test ligand in a container to produce a control combination;

(d) subjecting each of the test combinations and the control combination to conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent;

(e) measuring the extent to which the target protein occurs in the folded state, the unfolded state or both in the test combinations and in the control combination;

(f) repeating steps (a) through (e) rapidly with large numbers of said test ligands; and

(g) selecting as a lead compound any test ligand in a test combination in which the target protein is present in the folded state to a greater extent than in the control combination.

17. The method of claim 16 wherein the target protein is in a soluble form or bound to a solid phase matrix.

18. The method of claim 1 wherein said conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent comprise heating said control combination.

19. The method of claim 2 wherein said conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent comprise heating said control combination.

20. The method of claim 3 wherein said conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent comprise heating said control combination.

21. The method of claim 11 wherein said conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent comprise heating said control combination.

22. The method of claim 12 wherein said conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent comprise heating said control combination.

23. The method of claim 13 wherein said conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent comprise heating said control combination.

24. The method of claim 16 wherein said conditions sufficient to cause the target protein in the control combination to unfold to a measurable extent comprise heating said control combination.

25. The method of claim 18 wherein said test ligand comprises a small organic molecule.

26. The method of claim 19 wherein said test ligand comprises a small organic molecule.

27. The method of claim 21 wherein said test ligand comprises a small organic molecule.

28. The method of claim 22 wherein said test ligand comprises a small organic molecule.

29. The method of claim 23 wherein said test ligand comprises a small organic molecule.

30. The method of claim 24 wherein said test ligand comprises a small organic molecule.

31. The method of claim 1 which comprises measuring the extent to which the target protein is unfolded in each of the test and control combinations using fluorescence spectroscopy.

32. The method of claim 2 which comprises measuring the extent to which the target protein is unfolded in each of the test and control combinations using fluorescence spectroscopy.

33. The method of claim 3 which comprises measuring the extent to which the target protein is unfolded in each of the test and control combinations using fluorescence spectroscopy.

34. The method of claim 11 which comprises measuring the extent to which the target protein is unfolded in each of the test and control combinations using fluorescence spectroscopy.

35. The method of claim 12 which comprises measuring the extent to which the target protein is unfolded in each of the test and control combinations using fluorescence spectroscopy.

36. The method of claim 13 which comprises measuring the extent to which the target protein is unfolded in each of the test and control combinations using fluorescence spectroscopy.

37. The method of claim 16 which comprises measuring the extent to which the target protein is unfolded in each of the test and control combinations using fluorescence spectroscopy.

38. The method of claim 1, wherein one or more biochemical activities of said target protein are known or have been determined, further comprising the steps of:

contacting said selected ligand with said target protein under conditions suitable for assaying one or more biochemical activities of said target protein; and

determining if one or more of said biochemical activities of said target protein have been inhibited or augmented by said contacting.

39. The method of claim 2, wherein one or more biochemical activities of said target protein are known or have been determined, further comprising the steps of:

contacting said selected ligand with said target protein under conditions suitable for assaying one or more biochemical activities of said target protein; and

determining if one or more of said biochemical activities of said target protein have been inhibited or augmented by said contacting.

40. The method of claim 3, wherein one or more biochemical activities of said target protein are known or have been determined, further comprising the steps of:

contacting said selected ligand with said target protein under conditions suitable for assaying one or more biochemical activities of said target protein; and

determining if one or more of said biochemical activities of said target protein have been inhibited or augmented by said contacting.

41. The method of claim 11, wherein one or more biochemical activities of said target protein are known or have been determined, further comprising the steps of:

contacting said selected ligand with said target protein under conditions suitable for assaying one or more biochemical activities of said target protein; and

determining if one or more of said biochemical activities of said target protein have been inhibited or augmented by said contacting.

42. The method of claim 12, wherein one or more biochemical activities of said target protein are known or have been determined, further comprising the steps of:

contacting said selected ligand with said target protein under conditions suitable for assaying one or more biochemical activities of said target protein; and

determining if one or more of said biochemical activities of said target protein have been inhibited or augmented by said contacting.

43. The method of claim 13, wherein one or more biochemical activities of said target protein are known or have been determined, further comprising the steps of:

contacting said selected ligand with said target protein under conditions suitable for assaying one or more biochemical activities of said target protein; and

determining if one or more of said biochemical activities of said target protein have been inhibited or augmented by said contacting.

44. The method of claim 16, wherein one or more biochemical activities of said target protein are known or have been determined, further comprising the steps of:

contacting said selected ligand with said target protein under conditions suitable for assaying one or more biochemical activities of said target protein; and

determining if one or more of said biochemical activities of said target protein have been inhibited or augmented by said contacting.

45. A fluorescence-based screening method to identify a ligand that binds to a predetermined target protein, comprising the steps of:

(a) selecting as test ligands a plurality of compounds not known to bind to the target protein;

(b) incubating the target protein with each of said test ligands to produce a test combination, and in the absence of a test ligand to produce a control combination;

(c) contacting said test and control combinations with a fluorescence probe to measure the absolute amounts of folded and unfolded target protein, the folded:unfolded ratio, or the rates of folding or unfolding;

(d) subjecting said test and control combinations to unfolding conditions that cause a detectable fraction of the target protein to unfold in the absence of test ligand;

(e) measuring the fluorescence of said probe in said test and control combinations; and

(f) comparing the measurement made in step (e) between the test and control combinations, wherein if the fluorescence of said probe is greater or lesser in the test combination than in the control combination, the test ligand is a ligand that binds to the target protein.

46. The method of claim 45 further comprising repeating steps (b)-(f) with a plurality of said test ligands until a ligand that binds to the target protein is identified.

47. The method of claim 46, wherein said fluorescence probe binds preferentially to the folded or unfolded state of the protein.

48. The method of claim 45, wherein said subjecting comprises elevating the temperature to which said test and control combinations are exposed, contacting said test and control combinations with a denaturant, or combinations thereof.

49. The method of claim 45, wherein said target protein contains stabilizing or destabilizing amino acid substitutions relative to the wild-type version of said protein.

50. The method of claim 45, wherein said test ligand is selected from the group consisting of metals, peptides, proteins, lipids, polysaccharides, nucleic acids, small organic molecules, and combinations thereof.

51. A method for identifying compounds which bind to target proteins for use in developing new pharmaceutical agents, comprising the steps of:

(a) selecting as test ligands a plurality of compounds comprising compounds not known to bind to the target protein;

(b) incubating the target protein with each of said test ligands to produce test combinations, and in the absence of a test ligand, to produce a control combination;

(c) contacting said test and control combinations with a fluorescence probe to measure the absolute amounts of folded and unfolded target protein, the folded:unfolded ratio, or the rates of folding or unfolding;

(d) determining the extent to which the target protein occurs in the folded state, the unfolded state, or both, in the test combination and in the control combination subjected to unfolding conditions determined to cause a detectable fraction of the target protein to unfold in the absence of test ligand by observing a change in fluorescence of said probe;

(e) comparing the determinations made in the test and control combinations; and

(f) repeating steps (b) - (f) in a high throughput screening procedure until the comparison in step (f) identifies at least one compound, by indicating at least one test ligand that binds to the target protein.

52. The method of claim 51 which comprises repeating steps (b) - (f) with thousands of test ligands.

53. The method of claim 45 wherein the unfolding conditions induce the target protein to become denatured.

54. The method of claim 51 wherein the unfolding conditions induce the target protein to become denatured.

55. The method of claim 53 wherein the unfolding conditions are sufficient to at least partially denature the target protein.

56. The method of claim 54 wherein the unfolding conditions are sufficient to at least partially denature the target protein.

57. The method of claim 45 wherein the biochemical function of the target protein is unknown.

58. The method of claim 51 wherein the biochemical function of the target protein is unknown.

59. The method of claim 45 wherein the target protein comprises a polypeptide or protein implicated in the etiology of a disease.

60. The method of claim 51 wherein the target protein comprises a polypeptide or protein implicated in the etiology of a disease.

61. A high throughput screening method for identifying at least one compound from a test combination for possible development as a pharmaceutical agent, comprising the steps of:

(a) selecting as test ligands a plurality of compounds not known to bind to a target protein;

(b) placing at least one of the test ligands in a test well with the target protein to form a test combination;

(c) placing the target protein in a separate test well in the absence of a test ligand to form a control combination;

(d) contacting said test and control combinations with fluorescence probe to measure the absolute amounts of folded and unfolded target protein, the folded:unfolded ratio, or the rates of folding or unfolding;

(e) subjecting said test and control combinations to conditions determined to cause a detectable fraction of the target protein to unfold in the absence of test ligand;

(f) measuring change in the fluorescence of said probe to determine the extent to which the target protein occurs in the folded or unfolded state or both, in each of the test combinations and the control combination;

(g) identifying test combinations in which the target protein is present in the folded or unfolded state to a greater or lesser extent than in the control combination based on a change in the fluorescence measured in step (f); and

(h) selecting at least one test ligand in at least one of the identified test combinations.

62. The method according to claim 61 wherein said measuring step comprises determining the ratio of folded to unfolded target protein.

63. The method of claim 45 wherein the conditions in step (d) include an elevated temperature.

64. The method of claim 51 wherein the conditions in step (d) include an elevated temperature.

65. The method of claim 61 wherein the conditions in step (e) include an elevated temperature.